REMARKS

In the Office Action mailed on March 11, 2002, the Examiner rejected claims 1-6, 8-12, 14-15 and 17-20 and also objected to claims 7, 13 and 16. More particularly, the Examiner rejected claims 17-20 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner also rejected claims 1-3, 6, 9, 12, 14, 15, 17 and 18 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,246,866 to Nasu et al. ("Nasu"). Further, the Examiner rejected claims 1-4, 6, 8-10, 12, 14, 15 and 18 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,274,240 to Mathies et al. ("Mathies") in view of U.S. Patent No. 5,627,643 to Birnbaum et al. ("Birnbaum"). In addition, the Examiner rejected claims 5 and 11 under 35 U.S.C. §103(a) as being unpatentable over Nasu in view of U.S. Patent No. 5,637,458 to Frankel et al. ("Frankel"). Furthermore, the Examiner rejected claim 19 under 35 U.S.C. §103(a) as being unpatentable over Mathies in view of Birnbaum in further view of U.S. Patent No. 6,136,612 to Della Ciana et al. ("Della Ciana").

In addition, the Examiner objected claims 7, 13 and 16 as being dependent upon a rejected base claim, but indicated that the claims would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims. In particular, the Examiner noted that the prior art does not teach or suggest the claimed method or device with an amorphous silicon two-dimensional image sensor array. Furthermore, the Examiner noted that claim 20 is rejected under 35 U.S.C. §112, second paragraph, but free of the prior art, stating that there is no prior art that teaches or suggests the claimed device where the laser is attached to the rear of the detector.

In view of the amendments and remarks as set forth herein, Applicants respectfully submit that the pending claims, claims 1-20, are now in condition for allowance.

A. Rejection of Claims 17-20 Under §112

In the Office Action mailed on March 11, 2002, the Examiner rejected claims 17-20 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner rejected claims 17-20 stating that

the rejected claims recite the illumination means and depend on claim 14, but claim 14 does not recite an illumination means and, therefore, antecedent basis is lacking. Applicants submit that claim 14 has amended to include the illumination means to provide a proper antecedent basis for rejected claims 17-20. Exemplary support for an illumination source can be found within the specification at page 9, lines 5-12 which states that "[i]n order to image an object 116, the object 116 is illuminated by an illumination source 117 ..., which generates a fluorescent emission from the object."

Therefore, Applicants respectfully submit that claims 17-20 are now in condition for allowance. As such, Applicants respectively request that the Examiner remove all rejections to claims 17-20 under 35 U.S.C. §112, second paragraph, and allow the claims as written.

B. Rejection of Claims 1-3, 6, 9, 12, 14, 15, 17 and 18 Under §102(b)

The Examiner also rejected claims 1-3, 6, 9, 12, 14, 15, 17 and 18 under 35 U.S.C. §102(b) as being anticipated by Nasu. The Examiner stated that Nasu teaches a DNA sequencing apparatus in which fluorescently labeled fragments are subject to electrophoresis and illuminated and exposed to detection to create an image corresponding to the gel. Furthermore, the Examiner stated that Nasu teaches the apparatus with an electrophoresis unit (separation apparatus) with an upper electrode and a lower electrode, which applies an electric field to separate fragments and an optical sensor (detector) and optical source (illumination means). The Examiner stated that Nasu also teaches that the apparatus contains a gel which is a polymer solution and that the apparatus is attached to a processing unit which can create an image corresponding to the gel. The Examiner stated that the light receiving elements are arranged perpendicular to the direction of the electrophoresis and the image represents the same type of gel. Finally, the Examiner stated that Nasu teaches that the detector scans the full width of the array of samples in the gel and that detection occurs over several time periods. The Examiner also argued that the term "full width scanner" reads broadly and would encompass the detector in Nasu's device.

Applicants respectfully submit that the rejected claims are not anticipated by Nasu. In particular, claim 1 specifically calls for a method of

sequencing DNA fragments that includes separating the DNA sample into fragments along the migration channel within the buffer, detecting fluorescent light emitted from the fragments along the migration channel, and, generating a full image of the separation apparatus and the separated DNA fragments at a given time based on the detecting. Thus, the present invention provides a technique for sequencing an entire sequencing plate (or separation apparatus) holding DNA fragments using known methods of DNA sequencing in combination with a full-width scanner or a large area detector so that the image represents an entire sequencing plate at a given time. As stated in the specification, numerous advantages are achieved, including the provision of useful temporal data on the electrophoresis.

Nasu does not include each and every claimed element of the present invention. Specifically, the presently claimed subject matter (in independent claims 1, 9 and 14) calls for generating a *full image* of the separation apparatus and the separated DNA fragments *at a given time* based on the detecting, whereas Nasu describes constantly scanning in the direction of migration. (col. 5, ln. 56 – col. 6, ln. 2) In this regard, the Examiner indicates that the detecting in Nasu occurs over several time periods. As such, Applicants respectfully request that the Examiner remove all rejections to claims 1-3, 6, 9, 12, 14, 15, 17 and 18 under 35 U.S.C. §102(b), and allow the claims as amended.

C. Rejection of Claims 1-4, 6, 8-10, 12, 14, 15 and 18 Under §103(a)

The Examiner also rejected claims 1-4, 6, 8-10, 12, 14, 15 and 18 under 35 U.S.C. §103(a) as being unpatentable over Mathies in view of Birnbaum. The Examiner stated that Mathies teaches capillary gel electrophoresis for DNA sequencing and that Birnbaum teaches a capillary electrophoresis apparatus to separate fluorescence using an electric field. The Examiner also stated that Birnbaum teaches thin capillaries and a laser which irradiates samples along the capillary with a CCD detector for generating an electronic image of the appearance of the capillary along the direction of migration and detection occurring over various time intervals. The Examiner argued that one of ordinary skill in the art would have been motivated to apply Birnbaum's detection device in order to provide real-time detection of various labels simultaneously. Further, the Examiner argues that Birnbaum states that the whole capillary may be examined momentarily allowing for simultaneous detection

which provides a quicker evaluation. The Examiner argued that it would have been prima facie obvious to apply Birnbaum's device to detect in capillary electrophoretic devices in order to detect simultaneously and in real time the separation of DNA fragments.

Applicants respectfully submit that the teachings of Mathies in view of Birnbaum do not render the presently claimed subject matter obvious. For example, claims 1, 9 and 14 of the present application specifically calls for sequencing DNA fragments using a separation apparatus having a plurality of migration channels and generating a full image of the apparatus and the fragments at a given time.

In contrast, Birnbaum teaches a laser irradiation method for detecting separation of DNA fragments within a single thin capillary. The disclosure of Birnbaum specifically calls for a particular type of DNA fragment separation using laser irradiation through a capillary and then using, in a preferred form, a CCD detector in order to detect the separation of the DNA sample within the capillary. There is no suggestion in Birnbaum to use the presently claimed subject matter. That is, there is no teaching or suggestion to use the full width array detection at a given time that is called for by the presently claimed subject matter. Thus, while Birnbaum may disclose looking at an entire capillary, Birnbaum does not teach the use of a full-width image scanner in order to detect the progress of DNA fragment migration through the entire separation apparatus, having a plurality of migration channels, at a particular instance.

Furthermore, Mathies also does not teach or suggest a DNA sequencing method and apparatus as is presently claimed. Mathies teaches a method of analyzing a plurality of capillaries using a single scanner by scanning the plurality of capillaries in side-by-side relationship, and periodically and repetitively detecting fluorescence from each capillary passage during electrophoresis. In this regard, the Examiner indicates that Mathies does not teach full scan imagery. Indeed, Mathies appears to teach away from a full-width image detector. Specifically, at col. 9, lines 9-15, Mathies discloses that "continuous scanning [a]cross the capillary array" is preferred. Mathies goes on to state that "[i]n some applications, it may be desirable to focus sequentially at the center of each capillary and step between capillaries.", and also, that "it is possible to scan across each capillary to scan the band, but then rapidly step or move to the next capillary." Thus, Mathies does not contemplate the use of a

full-width scanner array for detecting the entire capillary as does the presently claimed subject matter.

Therefore, no combination of Mathies and Birnbaum would result in the claimed invention – which includes a generation of a full image of the apparatus and fragments therein for a given time. Furthermore, there is no motivation in Mathies for combining the teachings of Birnbaum of using a whole capillary detection system. The Examiner is applying impermissible hindsight in combining the two references. As such, Applicants respectfully request that the Examiner remove all rejections to claims 1-4, 6, 8-10, 12, 14, 15 and 18 under 35 U.S.C. §103(a) and allow the claims as amended.

The Examiner also rejected claims 5 and 11 under 35 U.S.C. §103(a) as being unpatentable over Nasu in view of Frankel. However, because it has been established that the claims from which claims 5 and 11 depend are distinguishable, claims 5 and 11 are also distinguishable from any combination suggested by the Examiner.

As such, Applicants submit that claims 5 and 11 are not obvious over Nasu in view of Frankel. Applicants respectfully request that the Examiner remove all rejections under 35 U.S.C. §103(a) of claims 5 and 11 and allow the claims.

In addition, the Examiner rejected claim 19 under 35 U.S.C. §103(a) as being unpatentable over Mathies in view of Birnbaum in further view of Della Ciana. However, claim 14 has already been established as distinguishable over the cited combination of Mathies and Birnbaum. Because claim 19 depends from claim 14 and the addition of Della Ciana does not change the arguments relative to claim 14, claim 19 is also distinguishable.

As such, Applicants respectfully submit that claim 19 is not rendered obvious over Mathies in view of Birnbaum in further view of Della Ciana. Therefore, Applicants respectfully request that the Examiner remove the rejection to claim 19 and allow the claim.

D. Objection of Claims 7, 13 and 16

In addition, the Examiner rejected to claims 7, 13 and 16 stating that they are dependent upon a rejected base claim, but would be allowable if rewritten in independent form to include all of the limitations of the base claim and any

intervening claims. The Examiner stated that there is no prior art that teaches or suggests the claimed method or device with an amorphous silicon two-dimensional image sensor array.

The Examiner also rejected claim 20 under 35 U.S.C. §112, second paragraph, but stated that that rejection is free of prior art. The Examiner stated that no prior art teaches or suggests the claimed device where the laser is attached to the rear of the detector.

In view of the remarks and amendments herein, Applicants submit that claims 7, 13, 16 and 20 are now in condition for allowance, and as such, the Applicants respectfully request that the Examiner remove all rejections and objections to those claims and allow the claims.

E. Conclusion

Applicants respectfully submit that the rejections and objections set forth by the Examiner in the Office Action of March 11, 2002, have been overcome. Accordingly, Applicants respectfully submit that claims 1-20 are now in condition for allowance. Withdrawal of the rejections and objections and early notification of allowability is earnestly solicited. Should any issues remain, the Examiner is encouraged to contact the undersigned to resolve any such issues.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 4, 5, 9, 10 and 14 have been amended as follows:

1. (Amended) A method of sequencing DNA fragments comprising:

placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

separating the DNA sample into fragments along the migration channel within the buffer;

detecting fluorescent light emitted from the fragments along the migration channel; and,

generating a full image of the separation apparatus and the separated DNA fragments at a given time based on the detecting.

4. (Amended) The method of claim 1 wherein the separation apparatus comprises [at least one] a plurality of capillary tubes forming the migration channels.

5. (Amended) The method of claim 1 wherein the separation apparatus comprises a set of glass plates with lithographically etched channels forming the migration channels.

9. (Amended) An apparatus for the sequencing of DNA comprising:

a separation apparatus having a plurality of migration channels operative to receive a DNA sample and facilitate migration and separation into fragments of the DNA sample along a migration channel within the apparatus;

a detector operative to detect light emitted [the] from DNA fragments along the migration channels; and,

an image processor operative to generate image data representing a full image of the separation apparatus and the DNA fragments at a given time.

10. (Amended) The apparatus of claim 9 wherein the separation apparatus comprises:

[at least one] a plurality of capillary tubes comprising the migration channels;

a buffer; and,

a means for providing an electric field to create a bias between ends of the capillary tubes.

14. (Amended) A system for sequencing DNA fragments comprising:

means for placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

means for applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

means for separating the DNA sample into fragments along the migration channel within the buffer;

means for illuminating the DNA fragments;

means for detecting fluorescent light emitted from the illumination fragments along the migration channel; and,

means for generating a full image of the separation apparatus and the separated DNA fragments at a given time based on the detecting.